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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,870	ROMANS, MARY H.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/11/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18,20,22,23,25 and 27* is/are pending in the application.

4a) Of the above claim(s) *10-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20,22,23,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *N/A* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/11/2005 has been entered.

Claims 1-9,19,21,24 and 26 have been cancelled. Claims 18,20,22,23,25 and 27 are amended. Claims 10-18,20,22,23,25 and 27 are pending. Claims 18,20,22,23,25 and 27 are under consideration in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claims 18-27 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, set forth in the final office action mailed 08/11/2004 is withdrawn in light of Applicant's amendments to the claims that remove terminology referring to non-transgenic.

Applicant has added terminology to claim 18 referring to the fascial tunnel. Applicant points to support in the specification for the "fascial tunnel" terminology at pages 15-16. While literal support for this terminology is not found, it has been determined that this terminology refers to the same location as that described in the specification and does not alter the scope of the claims.

A new grounds of rejection under written description appears below.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998).

Claim 27 broadly encompasses compression of the tibial nerve wherein allodynia, hyperalgesia or both result. The claimed mammal exhibiting hyperalgesia or exhibiting both hyperalgesia and allodynia have not been described in the instant specification. The specification provides description of only the claimed mammals exhibiting allodynia that are encompassed by the claims.

Therefore, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the genera of transgenic mice recited in the claims at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Enablement

The previous rejection of claims 18-27 as lacking enablement for the full breadth of the claims as set forth on pages 3-5 of the previous office action mailed 08/11/04 is withdrawn. However, a new scope of enablement rejection appear below as was indicated in the advisory action mailed 02/02/2005.

Claims 18,20,22,23,25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making a non-human mammal comprising non-surgically compressing the posterior tibial nerve such that allodynia is achieved and for the mammal made by said method, does not reasonably provide enablement for said method or product wherein any tibial nerve is altered or wherein hyperalgesia is achieved or wherein no effect is achieved. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered

in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Claims 18,19,23 and 25 broadly encompass compression of the tibial nerve wherein no effect occurs in the mammal. Claims 22 and 27 broadly encompasses compression of the tibial nerve wherein allodynia, hyperalgesia or both result. All claims encompass any tibial nerve including the anterior as well as the posterior tibial nerves.

The specification teaches that compression of the posterior tibial nerve results in allodynia but does not teach that such compression results in hyperalgesia. Hyperalgesia and allodynia are two distinct neurological effects. Stedman's Medical Dictionary defines hyperalgesia as "Extreme sensitivity to painful stimuli" (http://216.251.232.159/semdweb/internetsomd/ASP/1526727.asp) whereas it defines allodynia as "Condition in which ordinarily nonpainful stimuli evoke pain" (http://216.251.232.159/semdweb/internetsomd/ASP/1526727.asp). The stimulus that evokes each of the characteristics differs. There are no teachings in the specification that indicate that the presence of allodynia in the claimed mammals would also correlate to the presence of hyperalgesia. Therefore, it is not demonstrated that the mammal comprising an alteration of the tibial nerve caused by placing a gel substance in the tunnel around the nerve would exhibit hyperalgesia.

Claims 18,19,23 and 25 do not require that the mammal exhibit any effect as a result of the injected gel substance. The claims, therefore, encompass mammals that do not appear to differ in any manner from a wild-type mammal. Without some sort of phenotypic effect from the injected collagen, the skilled artisan would not know how to use the claimed mammal in any manner other than a wild-type mammal. Without some sort of phenotypic effect, it is not clear how the claimed mammal can be a model for persistent neurogenic pain as claimed.

The claims also encompass compression of the anterior tibial nerve. As set forth in the previous office action at page 4, the specification has demonstrated that compression of different nerves will result in different effects. The specification only teaches compression of the posterior tibial and saphenous nerves and the resulting effects for each. The specification does not teach the effects of compression of the anterior tibial nerve. It is not known if such compression would result in allodynia as observed with the posterior tibial nerve, or in hyperalgesia as described for compression of the saphenous nerve, or in some other effect.

Therefore, in light of the breadth of the claims encompassing both allodynia and hyperalgesia, the known characteristic distinction between allodynia and hyperalgesia and the lack of guidance in the specification with respect to the claimed mammal exhibiting hyperalgesia, it would require to make the mammals encompassed by the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 18 and 23 is withdrawn in light of Applicant's amendment to the claims requiring that the nerve alteration occur through non-surgical means. Reyna did not teach non-surgical placement of a gel into the tunnel comprising the tibial nerve.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18,22,23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyna (1999, ICLAS,Palma de Malloren, May 26-28, page 226).

Claim 18 is drawn to a method for producing a non-human mammalian model for persistent pain by altering the tibial nerve non-surgically by placing a gel substance in the tunnel through which the nerve passes. Claim 22 requires that the placement of the gel result in allodynia. Claim 23 is directed to the non-human mammalian model wherein a gel is placed into the tunnel through which the posterior tibial nerve passes. Claim 27 is directed to said model wherein the placement of the gel results in allodynia.

Reyna taught introducing a proprietary biocompatible, non-irritating substance near the tibial nerve, which constitutes a non-traumatic nerve alteration by surgically exposing the posterior tibial nerve. The plantar hind paws were then tested for allodynia, a physiologic change associated with persistent neurogenic pain (paragraph 2). Reyna did not teach non-surgical placement of the gel.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Reyna and non-surgically introduce the gel substance into the tunnel surrounding the posterior tibial nerve as it would be desirable to use a less invasive technique in making an mammal to be used as a model of pain. One of ordinary skill in the art would have a reasonable expectation of success of performing the technique non-surgically as the nerve alteration is the same and can be performed simply by identifying the nerve by palpating the tibial region of the mammal.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

2) Claims 20 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyna as applied to claims 18 and 23 above, and further in view of Ford (1986, Laryngoscope, Vol. 96, pages 1249-1257).

Claims 20 and 25 limits the gel substance of claims 18 and 23 to collagen.

Reyna taught introducing a proprietary biocompatible, non-irritating substance near the tibial nerve, which constitutes a non-traumatic nerve alteration by surgically exposing the posterior tibial nerve. The plantar hind paws were then tested for allodynia, a physiologic change associated with persistent neurogenic pain (paragraph 2). Reyna did not teach that the gel was a collagen gel.

However, Ford taught injection of bovine collagen into the vocal cords to correct glottic insufficiency. Ford taught that collagen is safe, effective, easily injected and well tolerated (Abstract, page 1248, col. 2, paragraph 2) and that it attracts the ingrowth of fibroblasts allowing for deposition of new collagen (Abstract).

Accordingly, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to make the claimed mammalian pain model as taught by Reyna wherein the proprietary substance taught by Reyna is replaced with the collagen taught by Ford. One of ordinary skill in the art would have been sufficiently motivated to replace the proprietary substance with collagen due to its properties of inducing minimal immune response from the host animal, easy use and its ability to recruit fibroblasts that secrete new host collagen around the nerve where it is placed. One of skill in the art would expect a reasonable degree of success in using collagen gel in place of the proprietary gel substance of Reyna because it appears that collagen would have the necessary gel properties to carry out the method and does not have any noxious properties.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

Joe Woitach
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